pts were given EMP and VBL. Twenty-eight (37%) pts were given EMP only. Gleason pattern scores ranged from 4 (n=3), 4-7 (n=49), and 8-10 (n=23). Pre-treatment prostate specific antigen (PSA) was as follows: < 20 in 25 pts (33%), 21 to 50 in 28 pts (37%), and > 50 in 22 pts (29%). 47 pts (62%) were T2, 21 pts (28%) T3, and 7 pts (10%) T4. The median age was 77 years. All pts were treated with mega-voltage external beam radiation with a dose of 65 to 70 Gy in 7-71/2 weeks. Oral EMP 450 mg/m2 daily and VBL 3 mg/m2 weekly were given concomitantly in 47 pts. The remaining 28 pts received EMP only.

Results: Pronounced tumor regression was achieved in all pts at 6 weeks following the completion of the combined treatment. The serum PSA fell to an undetectable level in 81% of pts (61 out of 75) in 6 weeks. The long-term results with the median follow-up time of 63 months show that 80% of T2, 50% of T3 and 40% of T4 pts are free from the biochemical relapse (PSA > 4 ng/ml). In particular, the tumor control rate was impressive for those with the serum PSA 21-50, achieving a 74% freedom from the biochemical relapse. Importantly, there was no increased acute and late normal tissue morbidity from the combined regimen.

Conclusion: The long-term follow-up study of the combined EMP and EBRT confirms our earlier findings that the combined regimen is highly effective in achieving a durable tumor control in pts with locally advanced prostate cancer. Unlike other cytotoxic chemotherapeutic drugs, the combined treatment did not produce any disproportionately enhanced normal tissue toxicity.

534 POSTER DISCUSSION

External beam radiotherapy with high dose rate (HDR) brachytherapy boost in localised prostate cancer

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Purpose: To retrospectively analyse the outcome for patients (pts) with localised prostate cancer treated with conformal external beam radiotherapy (EBRT) in combination with HDR brachytherapy (BT).

Patients and Methods: Since 1988, 290 pts with localised prostate cancer (T1a-3b) have been treated with a combination of EBRT and BT in our hospital. EBRT was given with 2 Gy fractions to a total dose of 50 Gy. BT was given in two 10 Gy fractions. A remote afterloading technique was used with a HDR Ir-192 source. From 6 to 21 needles were inserted transperineally guided by transrectal ultrasound.

Data from 128 pts treated from 1988 to 1997, were analysed: The mean as well as median age was 64 years (range 50-77). Median follow-up time was 57 months (range 12-155). Preirradiatory androgen ablation therapy was given to 68 pts (50%). The tumour was classified as T1 in 16 pts (12%), T2 in 90 (70%), and T3 in 22 pts (17%). Pre-treatment PSA was available in 125 pts (98%) (range 1.2-93). PSA was <10 in 67 pts (52%), 10-20 in 29 (23%), and >20 in 29 pts (23%). Tumour pathological grade was low (Gleason score 2-4) in 37 pts (29%), intermediate (5-7) in 76 pts (59%), and high (8-10) in 15 pts (12%).

Results: At three years, the biochemical no evidence of disease rate (bNED) was 90%. Overall bNED was 83%. The bNED for pts with T1, T2, and T3 tumours was 81%, 86%, and 72% respectively. The overall bNED for pts with pre-treatment PSA <10, 10-20, and >20 was 90%, 79%, and 69% respectively. According to the histological grading the bNED was 86%, 83%, and 73% for low, intermediate and high grades. Disease progression was seen in 22 patients (17%). Local recurrence developed in 3 pts and metastatic disease in 9 pts. Eleven pts had biochemical failure only. Late severe complications were few. Urethral strictures requiring surgical intervention were seen in 9 pts.

Conclusion: Treatment results after conformal EBRT combined with HDR BT in patients with localised prostate cancer are promising.

535 POSTER DISCUSSION

Oncologists' perceptions and treatment practice variations in the treatment of hormone-refractory prostate cancer (HRPC): a pilot multinational study

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Purpose: To examine differences in the treatment practices, and perceptions of hormone-refractory prostate cancer therapy in different countries worldwide.

Methods: A written questionnaire was sent to medical oncologists and urologists in 21 countries (Canada, USA, Austria, Finland, France, Germany, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Slovak Republic, Spain, UK, Australia, Argentina, Brazil, Japan, Russia, South Africa) to assess aspects of HRPC including: current national guidelines and screening programs, clinical management of HRPC, historical trends, and reimbursement issues. All data were stratified by country and major geographical location and analyzed using the Fisher's Exact Test.

Results: Fifty-three oncologists from the 21 surveyed countries completed the questionnaire. The oncologists were categorized by major geographic location: North America (n=12), Europe (n=26), Australia (n=4), South America (n=5), Japan (n=3), and Other (n=3). In most cases, guidelines and screening programs are not nationally regulated or mandated. In Japan primary screening for prostate cancer is commonly performed through the health check-up system. Secondary hormone therapy is the current standard therapy for HRPC in all groups. Pain control was rated the most important parameter in first-line treatment option decisions in most groups. Most notably exceptions to this were Japan where patient satisfaction was rated the highest, and North America where median survival benefits was considered the most important. However, in both cases, pain control was the next most important parameter identified. For second-line treatment option decisions, all groups, except for Japan where patient satisfaction was again rated highest, ranked pain control most important. Moreover, 92% of the clinicians surveyed reported that quality of life evaluations were not routinely conducted. Doctors/prescribers were identified as having the most influence on the introduction and use of a new treatment in all groups, except for Japan in which health care organizations were identified as most influential.

Conclusions: For the majority of parameters assessed in this survey, the data collected from each groups was homogenous. However, Japan consistently differed from all other groups, especially in terms of importance of patient satisfaction and pain control in their treatment decision process.

Breast cancer: New drugs/regimes

536 POSTER DISCUSSION

An eight weeks dose-dense versus a 24 weeks sequential adriamycin/docetaxel combination as preoperative chemotherapy (CHT) in operable breast cancer (T2-3, N0-2,M0)

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In a previous phase II b - trial including 248 patients (P) we demonstrated that dose-dense CHT in the preoperative setting (ADOC: adriamycin 50mg/m2 + docetaxel 75 mg/m2 q 14d x 4 + G-CSF + Tamoxifen) results in a pathological complete response (pCR) - rate of 9.7%. In this current randomized study in P with cT2-3, cN0-2,M0 untreated breast cancer we want to demonstrate that this dose-dense schedule obtains a similar pCR - rate as a sequential schedule (AC-DOC: adriamycin 60 mg/m2 + cyclophosphamide 600 mg/m2 q 21d x 4 followed by docetaxel 100 mg/m2 q21d x 4) prior to surgery. Tamoxifen (20 mg/d for 5 years.) was given simultaneously in all P.

Within 22 months 728 of 1000 planned P have entered this trial. Median age was 52 years; median initial tumour diameter by palpation and by best appropriate imaging method was 4 cm and 2.8 cm, respectively; 60.7% had no palpable axillary lymphnodes. So far data on toxicity are available for 197 pts (ADOC 101, AC-DOC 96), i.e. the 4 or 8 cycles have been given completely.

Grade III/IV Toxicity	ADoc (% of P)	AC (% of P)	AC-Doc (% of P)
Anaemia	2	2	2
Neutropenia	32	61	55
Thrombopenia	0	2	1
Nausea	4	10	2
Skin	4	2	9
Nail	1	0	7
Alopecia	91	92	99
Infections	5	2	0
Neurotoxicity	1	0	4

No grade III/IV fluid retention or cardiac events were observed. Therapy was stopped preterm in 36 P (ADOC 17, AC-DOC 19) because of toxicity (17 P), progression (4 P), death (1 P), other causes (5 P), and for lack of compliance (9 P). In 26 of 193 (13.5%) P a pCR with no detectable viable tumor cells was confirmed.

Conclusion: Dose-dense combination or conventional sequence of adriamycin and docetaxel are feasible, well tolerated, and highly effective as preoperative CHT in primary operable breast cancer. The trial is planned to close in September 2001.

537 POSTER DISCUSSION

Preoperative trastuzumab (T) and paclitaxel (P) for HER2-overexpressing (HER2+) stage II/III breast cancer

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We conducted a phase II study of preoperative T&P, followed by definitive breast surgery and postoperative doxorubicin/cyclophosphamide (AC). The primary study endpoint was pathological complete response to preoperative therapy, defined as absence of invasive disease. Eligible women had HER2+ breast cancer (either +2 or +3 by IHC), clinical stage II or III disease, and LVEF > 50%. Preoperative treatments were T (4 mg/kg x 1, then 2 mg/kg weekly x 11) and P (175 mg/m2 every 3 weeks x 4 treatments). Adjuvant AC at standard doses of 60/600 mg/m2 respectively, every 3 weeks x 4, was begun after surgery and no less than 6 weeks after the final T dose. Cardiac function was assessed at baseline, following preoperative T&P, and after cycles 2 and 4 of AC. 40 patients (median age 49) were accrued to the study, having clinical stage II (55%) or III (43%) cancer (one patient had ipsilateral supraclavicular node involvement as sole site of metastatic disease). Initial biopsies were HER2 positive, 2+ (20%) or 3+ (80%). Asymptomatic grade 2 cardiac toxicity was seen in 4 patients, 1 following H&T, 3 during AC therapy. All 4 patients developed LVEF between 40 and 50%. One patient came off study following first T dose for hypersensitivity reaction. No other unexpected toxicity was observed. Pathological complete response was observed in 7 of 40 patients (18%). Objective clinical response (CR and/or PR) was observed in 27 of 40 patients (68%). Neoadjuvant T & P appears feasible in women with stage II/III HER2+ breast cancer, and has substantial clinical activity, particularly among women with HER2 3+ tumors. Cardiac function merits close surveillance in patients receive preoperative T & P followed by adjuvant AC.

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538 POSTER DISCUSSION

Efficacy and safety of three-weekly herceptin with paclitaxel in women with her2-positive metastatic breast cancer: preliminary results of a phase II trial

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Herceptin in combination with chemotherapy has been shown to increase survival in women with HER2 positive metastatic breast cancer (MBC). Herceptin has so far been administered weekly in most studies. A less frequent, 3-weekly treatment schedule would be more convenient for patients, doctors and treating institutions.

In this phase II study, patients received Herceptin at a dose of 8 mg/kg (loading) followed by 6 mg/kg every 3 weeks (maintenance) in combination with paclitaxel (175 mg/m2) every 3 weeks for 8 cycles. At this point, Herceptin was continued as monotherapy until progression of disease.

32 patients were recruited with a median age of 53 years (31-70). The majority (94%) of patients had metastatic disease: 50% lung metastases, 47% liver metastases and 19% a malignant pleural effusion at baseline. 81% of patients had 2 or more sites or organs involved. 68% had received previous treatment for MBC; 70% anthracyclines, 59% hormone therapy and 72% radiotherapy; 90% of patients were taxane naïve.

The median number of cycles (range) for paclitaxel was 6 (1-8) and for Herceptin 7 (1-22), counting 3 weekly doses as a cycle for Herceptin. 3 patients experienced infusion reactions during Herceptin infusion but were able to continue treatment. No serious cardiac events were reported: 5 patients experienced a decrease of more than 15% of their LVEF. The most common moderate to severe adverse events were (% of patients): myalgia (44%), arthralgia (31%), dyspnoea (16%), fatigue (6%), mucositis (6%), paresthesia (6%), headache (9%) and diarrhoea (9%). Grade 3 and 4 haematological toxicity was limited to neutropenia (grade 3, 13% of patients; grade 4, 3%).

Investigator assessed responses were: complete response 9.4%, partial response 43.8% and overall response rate 53% (95% CI 35-71); 25% of patients had stable disease. The median response duration was 6.3 months (1.5-13.4+) and 15 patients continue on treatment; the estimated median TTP is 10.9 months.

Preliminary data indicate that the efficacy and safety of this 3-weekly regimen of Herceptin with paclitaxel are similar to the standard, approved weekly regimen of Herceptin with paclitaxel (NEJM 2001;344;783-92). Further investigation of this 3-weekly Herceptin regimen is ongoing/planned in the metastatic setting (monotherapy) and it will be used in the HERA adjuvant study.

539 POSTER DISCUSSION

Cyclophosphamide (C) - Epirubicine (E) - Capecitabine (X) combination, CEX: A safe and active regimen in the treatment of locally advanced/inflammatory (LA/I) or large operable (LO) breast cancer (BC). An EORTC-IDBBC study

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Purpose: To evaluate the maximum tolerated dose (MTD) of X in combination with fixed doses of E (100 mg/m^2) and C (600 mg/m^2) q 3 weeks. To have preliminary information on the antitumor activity of the regimen by treating a cohort of 15 LA/I or LO BC patients (pts) at the MTD, for a maximum of 6 cycles.

Methods: Four dose-escalation levels (L) of X were planned: L1: 1500, L2: 1800, L3: 2100 and L4: 2400 mg/m^2/day from day 1 to day 14. Dose escalation was allowed if $\leq$1/3 or 1/6 pts experienced dose-limiting toxicity (DLT: febrile neutropenia: grade 4 neutropenia lasting $\geq$7 days; grade 4 thrombocytopenia; grade 3–4 non-hematological toxicity (NHT) other than alopecia; discontinuation of X for more than 8 doses due to toxicity). Eligible pts were $\geq$18 and $\leq$70 years old, had LA/I or LO BC and a WHO performance status (PS) 0–1.

Results: From February to December 2000, 23 pts entered the study (L1 = 3 pts; L2 = 3 pts; L3 = 15 pts: L4 = 2 pts). Major pts characteristics were: median age 48 years (range 33–68), PS 0 (23 pts): LA/1 BC (9 pts/9 pts); LO BC (5 pts). The MTD was identified at L3 since 2/2 pts treated at L4 experimented a DLT [grade 3 mucositis (1 pt) and grade 3 fatigue that led to X discontinuation for more than 8 doses (1 pt)].

Dose Level 3. *Drug administration* (15 pts/61 cycles): median number of cycles: 4. range 2–6; median relative dose intensity: 100%, 100%, and 96% for C, E, and X, respectively. *Safety data* (15 pts/60 cycles): G4 neutropenia (9 pts); febrile neutropenia (2 pts); no grade 4 NHT. Grade 3 NHT that occurred in >1 pts were nausea and palmar-plantar-crythrodysesthesia (2 pts each). *Activity data* (15/15 pts; WHO criteria): 1 CR; 10 PR; 4 NC. Median time to response was 44 days (range 30–83).

Conclusions: CEX is a safe regimen with a promising antitumor activity (RR 73%) in LA/1 and LO BC pts. Planned next step is to confirm the high activity of this association in a phase II trial.

540 POSTER DISCUSSION

A single, fixed-dose of Pegfilgrastim given once-per-chemotherapy cycle is as effecitve as daily Filgrastim in the management of neutropenia in high-risk breast cancer

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Purpose: Prophylactic use of Filgrastim (F) reduces the incidence and duration of chemotherapy-induced neutropenia (CIN), thereby decreasing the associated risk of infectious complications and compromised outcomes due to chemotherapy treatment delays and dose reductions. Pegfilgrastim (PegF) is a unique sustained-duration cytokine with self-regulating, neutrophil dependant pharmacokinetics. This randomized, double-blind,